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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/557,922	12/22/2005	Masao Mori	126068	4822

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OLIFF & BERRIDGE, PLC
P.O. BOX 320850
ALEXANDRIA, VA 22320-4850

EXAMINER	
ZAREK, PAUL E	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/557,922	MORI ET AL.	
	Examiner	Art Unit	
	Paul Zarek	4161	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 November 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/24/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-14 are currently pending. This is the first Office Action on the merits of the claim(s).

Election/Restrictions

2. Applicant's election with traverse of Group I and compound 6a in Fig 3. in the reply filed on 09/08/2008 is acknowledged. The traversal is on the ground(s) that the art cited in Office Action mailed on 08/12/2008 does not read on an embodiment of Claim 1. Applicant is correct that compound 10 disclosed in Hattori does not, in fact, read on Claim 1. However, Hattori discloses compound 6, an anti-HIV agent possessing the same core structure as that claimed in the instant invention. Moreover, compound 6 possesses the following substituents (using the labeling scheme of the instant application): R_1 is $-CO(CH_2)_eCH_3$, where e is 0, R_2 is $-CO(CH_2)_nCH_3$, wherein n is 8, and R_3, R_4, and R_5 are –H. The invention as claimed lacks a special technical feature. The requirement of a species election is vacated. Claims 1-5 and 7-14 read on the elected Group. Claim 6 is withdrawn as being drawn to a non-elected Group.

The requirement is still deemed proper and is therefore made FINAL.

Priority

3. Applicant's claim for the benefit of a prior-filed international application JP03/06422 (filed on 05/22/2003) under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. The effective filing date of the instant application is 05/22/2003

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Hattori (US Patent No. 6,268,395, provided in IDS).

6. Claim 1 of the instant application is drawn to an antiviral preparation comprising formula 1, having the substituents R_1, R_2, R_3, R_4, and R_5. The composition must have a safety index of 10 or more, as defined by assays in MT-4 cells. Claim 4 limits the antiviral preparation comprising formula 1, wherein R_1 is $-CO(CH_2)_eCH_3$, and e is a number between 0 and 12.

7. Hattori teaches an phorbol-derivative anti-HIV composition wherein R_1 is $-CO(CH_2)_eCH_3$, where e is 0, R_2 is $-CO(CH_2)_nCH_3$, wherein n is 8, and R_3, R_4, and R_5 are –H (compound 6). Compound 6 was assayed in MT-4. It possessed an IC_{100} (the concentration to fully inhibit the cytopathic effect) of 0.0076 μg/mL, and a CC_0 (minimum cytotoxic concentration) of 62.5 μg/mL. The CC_0/IC_{100} was 8220. This method of determining safety and

efficacy differs slightly from that of Claim 1 of the instant application in that the instant application requires a CC_{50}/EC_{50} of more than 10. It is reasonable to assume that the CC_{50} disclosed in Hattori would be double the concentration, of CC_{100}, which would equate to 125 μg/mL. The EC_{50} would be half the IC_{100}, which would give an EC_{50} equivalent of 0.0038 μg/mL. Then, the calculated CC_{50}/EC_{50} would be 32,895. Therefore, Hattori anticipates all the limitations of the rejected claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 2, 3, and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hattori.

11. Claim 2 limits R_1 of formula 1 to $(CH_2)_aX(CH_2)_bCH_3$, wherein X is O or S, a is a number of 1 to 3, and b is a number of 0 to 5. Claim 3 limits R_1 to $(CH_2)_cX(CH_2)_dYCH_3$, wherein X and Y are either O or S, c is a number of 1 to 3 and d is a number of 1 to 5. Claim 5 limits R_1 to $(CH_2)_fCH_3$, wherein f is a number of 0 to 5.

12. Hattori teaches a phorbol-derivative compound that has anti-HIV activity that is similar to derivatives claimed in Claims 2, 3, and 5. The difference between compound 6 taught by Hattori and the those claimed in Claims 2, 3, and 5 is that Hattori discloses a derivative of formula 1 wherein R_1 is either H or an ester. The instant claims limit R_1 to ether or thioether (Claim 2), diether or dithioether (Claim 3), or an alkyl group (Claim 5). Alkyl groups, esters and ethers are known to be protecting groups, and are considered obvious variants of each other. The prior art teaches an ester at R1, thereby rendering the alkyl, ether, diether, thioether, and dithioether groups of instant Claims 2, 3, and 5 obvious. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the anti-HIV compound taught by Hattori by introducing protecting groups (i.e. methoxymethyl, methoxyethoxymethyl, or alkyl) to prevent *in vivo* degradation of the compound. (Do not agree wityh this rejection. Claim 5 could be rejected over Hattori under the principle of homology ----- difference between the R1 of Hattori and applicants compound being a difference between a hydrogen and a methyl group, when f = 0). Any better?

13. Claims 7-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hattori as applied to claims 1 and 4 above and in further view of Raffanti and Haas (Goodman & Gilman's The Pharmaceutical Basis of Therapeutics, 2001).

14. Claim 7 of the instant application is drawn to an anti-HIV virus preparation comprising a phorbol derivative of formula 1 and at least one other agent having an anti-HIV effect. Claims 8-14 limit the other anti-HIV agent.

15. Hattori teaches an effective anti-HIV compound (compound 6) as described above. Hattori does not teach a composition in which the phorbol derivative is combined with a second anti-HIV agent.

16. Raffanti and Haas teach that "[a] central principle of therapy is to inhibit viral replication as completely and durably as possible . . .. This requires administering multiple drugs simultaneously" (pg 1351, col 1, "General Principles of Antiretroviral Thearpy). Anti-HIV drugs are well known in the art, including nucleoside reverse transcriptase inhibitors (NRTIs, i.e. Zidovudine), non-nucleoside reverse transcriptase inhibitors (NNRTIs, i.e. Nevirapine), and protease inhibitors (PIs, i.e. Saquinavir). Raffanti and Haas also teach the various sites of inhibiting HIV (Fig 51-1). What are the anti HIV agents taught by Raffanti and Haas. Further why cant you break this rejection into 2 ------- Hattori in view of Raffanti and Hattori in view of Haas? Raffanti and Haas is one reference with only 2 authors. If there are more than 2, I would have done Raffanti, et al.

17. Further, it is obvious to combine two drugs that are known to have the same effect, in this case, treating HIV infection. "'It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art.' *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980)" Therefore, it would have been *prima facie*

obvious to one of ordinary skill in the art at the time the invention was made to combine compound 6, which is taught by Hattori, with other drugs that are known to inhibit various aspects of HIV infection.

Conclusion

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617